Characterization of Dissolved-Phase Xenon-129 Properties in the Human Lung

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Target audience: Imaging scientists and physicians interested in hyperpolarized xenon-129 (Xe129) MRI and characteristics of pulmonary gas uptake/exchange.

Introduction & Purpose: Recent studies in humans have demonstrated that direct imaging of hyperpolarized Xe129 dissolved in lung tissue and blood plasma, and in the red blood cells (RBCs), has great potential for exploring fundamental characteristics of lung function, such as gas exchange and uptake [1,2]. While the chemical shifts associated with the two primary components of dissolved-phase Xe129 in the lung (RBCs and tissue/plasma) are well known, and the T2* value for the total dissolved phase at 1.5T has been measured at approximately 2 ms [3], typical values for the T2* of the individual components, as well as their relative fractions, are not well established. The purpose of this study was to determine, from whole-lung measurements, the fractions and T2* values for the RBC and tissue/plasma components of dissolved-phase Xe129 for healthy and diseased subjects, and to explore their dependence on the degree of lung inflation.

Methods: Dissolved-phase Xe129 free-induction decays (FIDs) were collected from two types of pulses sequences: (1) at the end of a 3D dissolved-phase/gas-phase image acquisition, an FID was collected with flip angle (FA) 23°, readout duration 54 ms, and start time 0.74 ms; and (2) as part of a Chemical Shift Saturation Recovery (CSSR) [4] acquisition, FIDs were acquired 100 ms after saturation of the dissolved-phase with FA 40-50°, readout duration 31 ms, and start time 0.7ms. Excitation RF pulses were applied 3660 Hz above the gas-phase resonance frequency. Studies were performed at 1.5T (Avanto; Siemens), using a flexible (Clinical MR Solutions) or rigid (custom built) Xe129 chest RF coil, under a physician's IND for Xe129 MRI. Informed consent was obtained in all cases and a physician supervised each study. Enriched xenon gas (87% Xe129) was polarized using a prototype commercial system (XeBox-E10, Xemed).

For acquisition type 1, FIDs were collected from 5 healthy nonsmoking subjects (H1-H5, H3 imaged twice), 1 healthy subject who had smoked for 15 years (S1), 2 with smoking-related COPD (GOLD Stage III, S2 [imaged twice] and S3) and 2 asthmatics (A1 [imaged twice] and A2) after each subject inhaled a gas volume equaling 1/3 of the subject's forced vital capacity (FVC) as determined by spirometry. For acquisition type 2, FIDs were collected from 3 healthy subjects (H6-H8) at three lung-inflation levels: (a) residual volume (RV), (b) after inhaling a gas volume of 1/2 FVC from RV, and (c) total lung capacity (TLC).

The complex FIDs were fitted to a bi-exponential decay model using 1stOPT (7D Soft High Tech. Inc., Beijing China). Parameters included T2* values, resonance frequencies, and fractions for the tissue/plasma and RBC components, and an initial phase difference between the components.

Results: All complex FIDs were fitted well, as indicated by an average R^2 value of 0.994. Corresponding spectra based on the fitted parameters were likewise very close to the original spectra. The quality of the fitting results is illustrated Fig. 1, showing examples from healthy subject H3 and COPD subject S2. Table 1 lists the fit parameters obtained from acquisition type 1. The resonance frequencies for both components were relatively consistent. RBC fractions found in most healthy subjects were higher than those for most diseased subjects (p=0.045). Subject S1, a long time smoker but clinically healthy, had an RBC fraction in the range of healthy values. Subject A2, a young asthmatic, had an RBC fraction higher than those for all of the healthy subjects. However, none of the healthy subjects in this study were as young as subject A2. Among the healthy subjects, T2* values of the RBC and tissue/plasma components were found to be consistent at 1.8-1.9 ms and 2.2-2.3 ms, respectively. Relative to healthy subjects, diseased subjects had slightly higher T2* values for the RBC components (p=0.024), and slightly lower T2* values for the tissue/plasma components (p=0.013). The effects of lung inflation level on RBC fraction, and RBC and tissue/plasma T2* values are shown in Table 2 for three healthy subjects. As the lung volume increased from RV to TLC, the RBC fraction decreased by approximately 30%. The T2* of the RBC component was relatively insensitive to lung inflation level, but the T2* of the tissue/plasma component decreased with increasing lung inflation.

Table 1. Fractions, resonance frequencies and T2* values for the RBC and tissue/plasma components obtained from fitting the dissolved-phase FID signals from acquisition type 1.

Sub	H1	H2	H3	H3*	H4	H5	S1	S2	S2*	S3	A1	A1*	A2
RBC Frac (%)	27	29	29	28	27	21	28	13	13	11	14	18	33
RBC Freq (Hz)	159	158	158	160	152	159	158	156	156	162	158	154	160
RBC T2* (ms)	1.8	1.8	1.8	1.8	1.9	1.9	1.9	2.2	2.2	2.2	2.2	2.0	1.7
Tiss Freq (Hz)	-181	-177	-174	-183	-177	-182	-182	-178	-178	-179	-176	-169	-174
Tiss T2* (ms)	2.2	2.2	2.2	2.2	2.3	2.2	2.1	2.0	2.0	2.1	2.2	2.2	1.9

Conclusions: In healthy subjects, the RBC fraction and T2*, and tissue/plasma T2*, showed little variation among subjects. The RBC fraction and tissue/plasma T2* were found to depend on the level of lung inflation. That the RBC fraction decreased with increasing lung volume suggests that gas exchange is reduced at high lung volumes. The RBC fraction was significantly lower in the diseased subjects than in healthy subjects. Both asthma and smoking-related lung disease are known to increase RV of the lung, that is, the lung volume at maximum expiration. An increase in RV would mean that lung volume at imaging of the diseased subjects was effectively larger than for healthy subjects, and could at least partially explain the decreased RBC fraction found in diseased subjects. However, the RBC fraction in diseased subjects was much lower than in healthy subjects at maximum inspiration (TLC), suggesting that factors other than just lung inflation level may cause impaired gas exchange.

References: 1. Cleveland ZI et al. Plos ONE 5(8): e12192. **2.** Mugler JP 3rd et al. PNAS USA 2010; 107(50): 21707. **3.** Mugler JP 3rd et al. ISMRM 2012; 1347. **4.** Patz S, et al. Acad Radiol 2008; 15(6):713. **Acknowledgement:** Supported by R01 HL109618 and Siemens Medical Solutions.

Table 2. RBC fraction and T2* values corresponding to the three lung-inflation levels (RV, 1/2 FVC and TLC) for acquisition type 2.

Subject	H6			H7			H8		
Inflation Level	RV	1/2FVC	TLC	RV	1/2FVC	TLC	RV	1/2FVC	TLC
RBC Frac (%)	36	31	23	35	31	24	29	20	20
RBC T2* (ms)	1.7	1.7	1.7	1.8	1.7	1.7	1.8	1.7	1.7
Tiss T2* (ms)	2.3	2.0	2.0	2.3	2.1	2.0	2.4	2.1	2.1

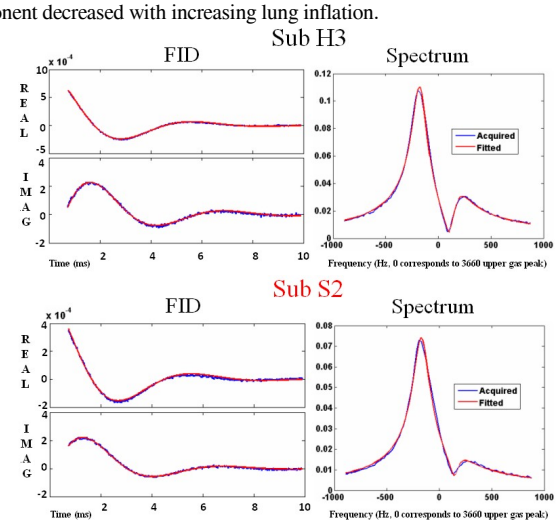

Figure 1. Fitted FIDs and corresponding spectra from healthy subject H3 and COPD subject S2. Blue shows the acquired data, red shows FIDs and spectra calculated based on fitting results.